

PATENT COOPERATION TREATY

From the
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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year)

18 SEP 2008

Applicant's or agent's file reference

27989

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/IL04/00577

International filing date (day/month/year)

29 June 2004 (29.06.2004)

Priority date (day/month/year)

30 June 2003 (30.06.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC: A61K 39/00(2006.01)

USPC: 424/184.1

Applicant

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1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/US
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Facsimile No. (571) 273-3201

Date of completion of this opinion
11 September 2008 (11.09.2008)

Authorized officer
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Form PCT/ISA/237 (cover sheet) (April 2007)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/IL04/00577

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).2. ☐ This opinion has been established taking into account the rectification of an obvious mistake authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a)).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this opinion has been established on the basis of:

a. type of material

☒ a sequence listing☒ table(s) related to the sequence listing

b. format of material

☒ on paper☐ in electronic form

c. time of filing/furnishing

☒ contained in the international application as filed.☐ filed together with the international application in electronic form.☐ furnished subsequently to this Authority for the purposes of search.4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Form PCT/ISA/237(Box No. I) (April 2007)

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/IL04/00577

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application
- ☒ claims Nos. 12.14.31-39.49.68.81.98.106.127.143 and 150

because:

- ☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require an international search (*specify*):

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 12.14.31-39.49.68.81.98.106.127.143 and 150 are so unclear that no meaningful opinion could be formed (*specify*):
no CRF provided.

- ☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

- ☐ no international search report has been established for said claims Nos. _____

- ☒ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

- ☒ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).

- ☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☐ See Supplemental Box for further details.

Form PCT/ISA/237 (Box No. III) (April 2007)

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IL04/00577

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>Please See Continuation Sheet</u>	YES
	Claims <u>Please See Continuation Sheet</u>	NO
Inventive step (IS)	Claims <u>Please See Continuation Sheet</u>	YES
	Claims <u>Please See Continuation Sheet</u>	NO
Industrial applicability (IA)	Claims <u>Please See Continuation Sheet</u>	YES
	Claims <u>Please See Continuation Sheet</u>	NO

2. Citations and explanations:

Claims 1, 3, 5-11, 13, 15-18, 20-28 and 30 lack novelty under PCT Article 33(2) as being anticipated by Pispisa et al. A spectroscopic and molecular mechanics investigation on a series of AIB-based linear peptides and a peptide template, both containing tryptophan and a nitroxide derivative as probes. Biopolymers. 2000 Feb;53(2):169-81.

The Pispisa et al. reference teaches linear and cyclic Aib-based peptides or peptidomimetics, comprising L-amino acids (e.g., gly, asp, and trp) that meet the structural limitations of the claims (see especially pp.169-175). Thus, the peptides also inherently meet the functional limitations of the claims.

Claims 102, 104, 105, 109-113, 115 and 116 lack an inventive step under PCT Article 33(3) as being obvious over Pispisa et al. Pispisa et al. teach as set forth above but do not explicitly teach encoding nucleic acids. However, methods of determining the encoding nucleic acids from disclosed peptides/polypeptides are well established in the art. Thus, it would be obvious to arrive at the claimed invention from the disclosure of the Pispisa et al. reference.

Claims 40, 42-48, 52-60, 62, 63, 66, 67, 69-72, 74-80, 84-92, 94, 96, 97, 99 and 100 lack an inventive step under PCT Article 33(3) as being obvious over Pispisa et al. in view of Tsai et al. (218th ACS National Meeting, New Orleans, August 22-26, 1999, Meeting abstract - MED1-018).

Pispisa et al. teach as forth above but do not teach pharmaceutical compositions.

However, Tsai et al. teach that Aib containing peptidomimetics inhibit amyloid β -protein (A β) production at the gamma secretase level. Thus, it would be obvious to combine the teachings of the two references to arrive at the claimed invention.

Claims 118, 120-126, 130-138, 140, 141, 145, 147, 148, 152 and 154 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied in the immediately preceding paragraph and further in view of WO 99/27944 to Schenk. The Schenk reference teaches methods of "preventing or treating a disease characterized by amyloid deposition in a patient. Such methods entail inducing an immune response against a peptide component of an amyloid deposit in the patient. Such induction can be active by administration of an immunogen or passive by administration of an antibody or an active fragment or derivative of the antibody" (see p.3, for example). Thus, it would be obvious to combine the teachings of the two references to arrive at the claimed invention.

Claims 2,4,19,29,41,50,51,61,64,65,82,83,93,95,103,107,108,114,117,119,128,129,139,142,144,146,149,151,153 and 155-162 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the limitations of said claims.

Claims 1-11,13,15-30,40-48,50-67,69-80,82-97,99-105,107-126,128-142,144-149 and 151-162 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

Form PCT/ISA/237 (Box No. V) (April 2007)

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/IL04/00577**Supplemental Box**

In case the space in any of the preceding boxes is not sufficient.

V.1. Reasoned Statements:

The opinion as to Novelty was positive (Yes) with respect to claims

2,4,19,29,41,50,51,61,64,65,73,82,83,93,95,103,107,108,114,117,119,128,129,139,142,144,146,149,151,153 and 155-162

The opinion as to Novelty was negative (No) with respect to claims 1, 3, 5-11, 13, 15-18, 20-28 and 30

The opinion as to Inventive Step was positive (Yes) with respect to claims

2,4,19,29,41,50,51,61,64,65,82,83,93,95,103,107,108,114,117,119,128,129,139,142,144,146,149,151,153 and 155-162

The opinion as to Inventive Step was negative (NO) with respect to claims 1, 3, 5-11, 13, 15-18, 20-28, 30, 40, 42-48, 52-

60, 62, 63, 66, 67, 69-72, 74-80, 84-92, 94, 96, 97, 99, 100, 102, 104, 105, 109-113, 115, 116, 118, 120-126, 130-138, 140, 141, 145, 147, 148, 152 and 154

The opinion as to Industrial Applicability was positive (YES) with respect to claims 1-11, 13, 15-30, 40-48, 50-67, 69-80, 82-97, 99-105, 107-126, 128-142, 144-149 and 151-162

The opinion as to Industrial Applicability was negative (NO) with respect to claims NONE

Form PCT/ISA/237 (Supplemental Box) (April 2007)